REMARKS

Status of Claims

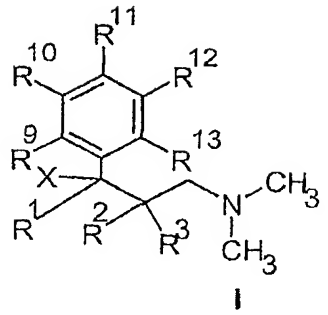
Claims 37-41, 48, 50-51, 54-57, and 73 are pending. Claim 37 is the only independent claim. Claims 38 and 40-41 are presently withdrawn. In this Reply, without conceding the propriety of the rejection and in order to expedite prosecution, independent claim 37 has been amended. Dependent claims 48, 50, 54, and 57 have been amended and claims 49 and 52-53 have been canceled to conform with the amendments to claim 37. Support for the amendments exists, *inter alia*, in the original claims. No new matter has been added. Applicants expressly reserve the right to file one or more divisional applications directed to subject matter deleted from the claims.

Applicants respectfully request the Examiner to reconsider and withdraw the rejections in view of the foregoing amendments and the following remarks.

Claim Rejection Under 35 U.S.C. § 103

The rejection of claims 37, 39, 48-51, 54-57 and 71-73 under 35 U.S.C. § 103(a) over Chutka et al., "Urinary Incontinence in the Elderly: Drug Treatment Options," 1998, Drugs, Volume 56, Number 4, pages 587-595 ("Chutka et al.") in view of U.S. Patent No. 6,248,737 ("Buschmann et al. '737") and Andersson et al., "The pharmacological treatment of urinary incontinence," 1999, British Journal of Urology International, 84:923-947 ("Andersson et al.") is respectfully traversed.

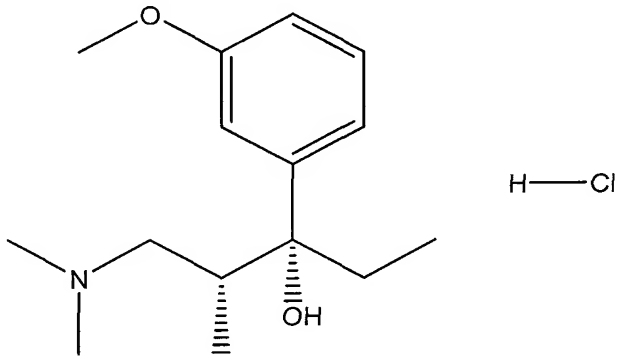
The presently claimed composition of matter of independent claim 37 comprises as an admixture at least one compound selected from group (i) and oxybutynin. Group (i) consists of 1-phenyl-3-dimethylamino-propane compounds corresponding to formula I, as depicted below, or salts thereof with a physiologically tolerated acid.



I

Formula I has been amended to encompass a relatively limited number of compounds. In amended formula I, X is OH. R^1 is chosen from C_{1-4}-alkyl, unbranched, saturated and unsubstituted. R^2 and R^3 in each case independently of one another are chosen from H or C_{1-4}-alkyl, unbranched, saturated and unsubstituted. R^9 to R^{13} in each case independently of one another are chosen from H and OR^{14}; where R^{14} is C_{1-6}-alkyl, unbranched, saturated and unsubstituted.

One of the compounds of formula I is (+)-(2*R*,3*R*)-1-dimethylamino-3-(3-methoxy-phenyl)-2-methyl-pentan-3-ol hydrochloride. This compound is shown below.



(+)-(2*R*,3*R*)-1-dimethylamino-3-(3-methoxy-phenyl)-2-methyl-pentan-3-ol hydrochloride was tested in Example 1 of the specification in combination with oxybutynin. As discussed in the previous Reply filed November 3, 2009, this combination exhibits an unexpected, synergistic effect in the treatment of ***urinary incontinence***. In Example 1, individual administration of the tested compound to rats provided 21.7% inhibition of the rate of bladder contractions

and individual administration of oxybutynin provided 10.7% inhibition of the rate of bladder contractions. In contrast, administration of the combination of the tested compound and oxybutynin provided 42.5% inhibition of the rate of bladder contractions. Thus, combined administration of the tested compound and oxybutynin provides a synergistic (i.e. supra-additive) effect.

The tested combination is representative of the presently claimed combination of at least one 1-phenyl-3-dimethylamino-propane compound of formula I and oxybutynin. As discussed above, formula I encompasses a relatively limited number of compounds. These compounds are very similar in structure. Accordingly, the tested compound is representative of the presently recited compounds of formula I and the unexpected, synergistic result for treating ***urinary incontinence*** associated with the tested combination is commensurate with the scope of the claims.

This unexpected, synergistic result, which is commensurate with the scope of the claims, effectively rebuts any *prima facie* case of obviousness over Chutka et al., Buschmann et al. '737, and Andersson et al.

Contrary to the Office Action's assertions, the probative value of the combination of the tested compound and oxybutynin can reasonably be extended to the narrowed group of structurally related compounds of formula I embraced by the amended claims. While Buschmann et al. '737 shows that the tested (+) enantiomer exhibits a pronounced ***analgesic*** effect greater than the ***analgesic*** effect of the (-) enantiomer, Buschmann et al. '737 does not disclose anything regarding the effectiveness of the tested compound for treating ***urinary incontinence***. Indeed, Buschmann et al. '737 discloses 1-phenyl-3-dimethylaminopropane compounds as ***analgesics suitable for the treatment of pain, not for the treatment of urinary incontinence***. Thus, Buschmann et al. '737's test data showing analgesic effect does ***not*** support the Office Action's assertion that the unexpected, synergistic effect with regard to treating urinary incontinence associated with the tested combination is not commensurate with the scope of the claims.

The test results of Example 1 are also commensurate with the scope of the claims even though only one dosage (0.1 mg/kg of the tested compound) and one dosage of oxybutynin (0.03 mg/kg) were tested. Applicants respectfully maintain that synergism is typically not dose dependent. Contrary to the Office Action's assertions, U.S. Patent No. 4,442,084 ("the '084 patent") does ***not*** show dose-dependent synergism. At col. 6, line 41-col. 7, line 17, the '084 patent provides test results for the combined activity of component A (1-isopropyl-4-(4-fluoro-phenyl)-7-methyl-2-(1H)-quinazolinone) and component B (5-chloro-4-(2-imidazolin-2-ylamino)-2,1,3-benzothiadiazole) at different relative dosages. At all relative dosages of the combination of component A and component B tested (i.e. test runs 2-4), the combination exhibited synergistic (i.e. super-additive) activity. This synergistic (i.e. super-additive) activity is shown in Figure 2. Applicants point out that Figure 1 merely shows three basic curves that could possibly be obtained. However, the curve actually obtained was the synergistic (i.e. super-additive) curve. Thus, the '084 patent supports Applicants' assertion that synergism is not typically dose dependent.

Because Applicants have demonstrated synergism for the presently claimed drug combination and one of ordinary skill in the art understands that synergism is not typically dose dependent, one of ordinary skill in the art would reasonably extend the probative value of the dosages tested in Example 1.

Therefore, for at least the reasons discussed above, withdrawal of the § 103(a) rejection over Chutka et al., Buschmann et al. '737, and Andersson et al. is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If there are any questions relating to this Reply or the application in general, it would be appreciated if the Examiner could telephone the

undersigned at (202) 624-2845 so that examination of this application may be expedited.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket # 029310.53299US).

Respectfully submitted,

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